

CLAIMS

1. A compound present in plants of the genus *Euphorbia*, and in particular in sap of *Euphorbia peplus*, *Euphorbia hirta* and/or *Euphorbia drummondii*, which:

5 (a) is able to kill or inhibit the growth of cancer cells, but does not significantly affect normal neonatal fibroblasts, or spontaneously transformed keratinocytes;

10 (b) has activity which is not destroyed by heating at 95°C for 15 minutes;

15 (c) has activity which is not destroyed by treatment with acetone;

(d) has activity which can be extracted with 95% ethanol; and

15 (e) stimulates metallothionein gene activation.

2. A compound according to Claim 1, which is able to inhibit the growth of at least one cell line selected from the group consisting of MM96L, MM229, MM220, MM537, MM2058, HeLa, B16, LIM1215, A549, MCF7, MCC16 and Colo16, as herein defined.

20 3. A compound according to Claim 2, which is able to inhibit growth of or to induce differentiation in MM96L cells.

4. A compound according to any one of Claims 1 to 3, 25 which is also able to induce normal melanocytes and/or T cells to proliferate.

5. A composition comprising a compound according to any one of Claims 1 to 4, together with a pharmaceutically- or cosmetically-acceptable carrier.

30 6. A composition according to Claim 5, in which the compound is selected from the group consisting of jatrophanes, pepluanes, paralianes and angeloyl-substituted ingenanes or acetylated derivatives thereof, and pharmaceutically-acceptable salts or esters thereof.

35 7. A composition according to Claim 6, in which the compound is a jatrophane of Conformation II.

24 JUN 1999

8. A composition according to Claim 6 or Claim 7, in which the compound is substituted as defined in Table 2.

9. A composition according to any one of Claims 5 to 8, in which the compound is selected from the group consisting of:

5 5,8,9,10,14-pentaacetoxy-3-benzoyloxy-15-hydroxypepluane (pepluane);

15-pentaacetoxy-9-nicotinoyloxy-14-oxojatropho-6(1),11E-diene (jatrophane 1);

10 2,5,7,9,14-hexaacetoxy-3-benzoyloxy-15-hydroxy-jatropho-6(17),11E-diene (jatrophane 2);

2,5,14-triacetoxy-3-benzoyloxy-8,15-dihydroxy-7-isobutyroyloxy-9-nicotinoyloxyjatropho-6(17),11E-diene (jatrophane 3);

15 2,5,9,14-tetraacetoxy-3-benzoyloxy-8,15-dihydroxy-7-isobutyroyloxyjatropho-6(17),11E-diene (jatrophane 4);

2,5,7,14-tetraacetoxy-3-benzoyloxy-8,15-dihydroxy-9-nicotinoyloxyjatropho-6(17),11E-diene (jatrophane 5);

2,5,7,9,14-pentaacetoxy-3-benzoyloxy-8,15-dihydroxyjatropho-6(17),11E-diene (jatrophane 6);

20 20-acetyl-ingenol-3-angelate;

and pharmaceutically-acceptable salts or esters thereof.

10. A composition according to any one of Claims 5 to 9, in which the carrier comprises β -alanine betaine hydrochloride or L-4-hydroxy-N,N-dimethyl proline.

25 11. A method of treatment of a cancer, comprising the step of administering an anti-cancer effective amount of a compound according to any one of Claims 1 to 4 or a composition according to any one of Claims 5 to 10 to a mammal in need of such treatment.

30 12. A method according to Claim 11, in which the cancer is a solid tumour.

13. A method according to Claim 11 or Claim 12, in which the cancer is selected from the group consisting of malignant melanoma, other skin cancers including Merkel cell carcinoma, squamous cell carcinoma and basal cell

carcinoma, lung cancer, colon cancer, prostate cancer, cervical cancer and breast cancer.

14. A method according to any one of Claims 11 to 13, used as an adjuvant to radiotherapy or to therapy with a 5 DNA-damaging agent.

15. A method of inhibiting proliferative activity of neoplastic cells, comprising the step of exposing the cells to an anti-proliferative amount of a compound according to any one of Claims 1 to 4, or a composition according to any 10 one of Claims 5 to 10.

16. A method of stimulating proliferation of non-neoplastic cells, comprising the step of exposing the cells to a proliferation-inducing amount of a compound according to any one of Claims 1 to 4 or a composition according to 15 any one of Claims 5 to 10.

17. A method of stimulating the activity and/or inducing proliferation of T-cells, comprising the step of exposing the cells to an effective amount of a compound according to any one of Claims 1 to 4, or a composition 20 according to any one of Claims 5 to 10.

18. A method of alleviating disease conditions by stimulating cells of the immune system, according to Claim 16.

19. A method of inducing neoplastic cells to 25 differentiate, comprising the step of exposing the cells to an effective amount of a compound according to any one of Claims 1 to 4, or a composition according to any one of Claims 5 to 10.

20. A method according to any one of Claims 15 to 18, 30 in which the cells are treated *in vivo*.

21. A method according to any one of Claims 15 to 18, in which the cells are treated *ex vivo*.

22. A method of preventing or alleviating damage to 35 skin caused by ultraviolet irradiation, ionizing radiation, microwave radiation or exposure to ozone, comprising the step of topically administering an effective amount of a compound according to any one of Claims 1 to 4 or a

composition according to any one of Claims 5 to 10 to a subject in need of such treatment.

23. A method according to Claim 22, in which the damage is solar keratosis.

5 24. A method according to Claim 22, in which the damage occurs during radiotherapy.

25. A method according to any one of Claims 11 to 24, in which the mammal is a human.

10 26. Use of a compound according to any one of Claims 1 to 4 in the treatment of cancer.

27. Use of a compound according to any one of Claims 1 to 4 for preventing or alleviating damage to skin caused by ultraviolet irradiation, ionizing radiation, microwave radiation or exposure to ozone

15 28. Use of a composition according to any one of Claims 5 to 10 in the treatment of cancer.

29. Use of a composition according to any one of Claims 5 to 10 in preventing or alleviating damage to skin caused by ultraviolet irradiation, ionizing radiation,

20 microwave radiation or exposure to ozone

30. Use of a compound according to any one of Claims 1 to 4, or a composition according to any one of Claims 5 to 10 in the manufacture of a medicament for the treatment of cancer.

25 31. Use of a compound according to any one of Claims 1 to 4, or a composition according to any one of Claims 5 to 10 in the manufacture of a medicament for preventing or alleviating damage to skin caused by ultraviolet irradiation, ionizing radiation, microwave

30 radiation or exposure to ozone.

32. Use of compound according to any one of Claims 1 to 4, or a composition according to any one of Claims 5 to 10 in the manufacture of a medicament for inducing proliferation of non-neoplastic cells.

35

add
A2

24 JUN 1999